

FIG. 1A

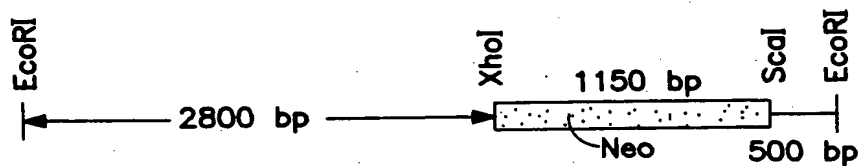


FIG. 1B

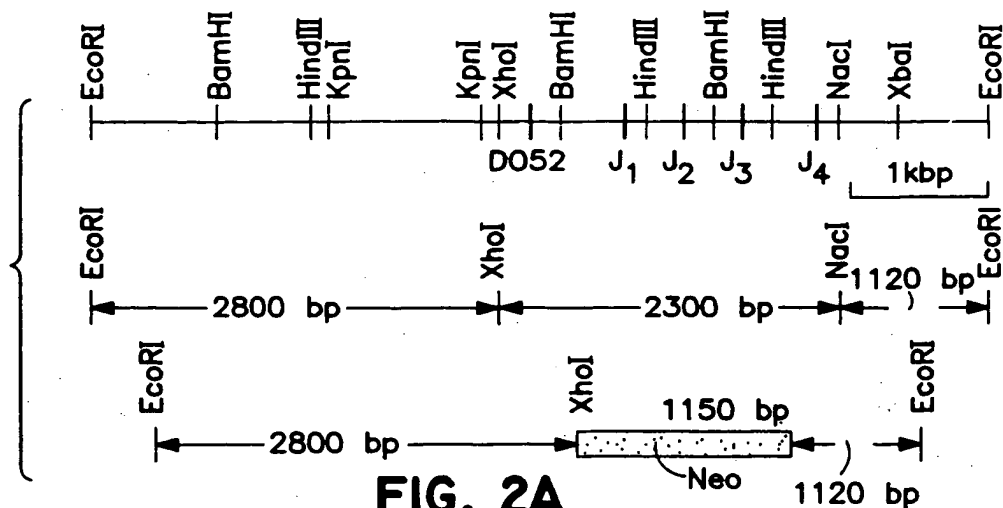


FIG. 2A

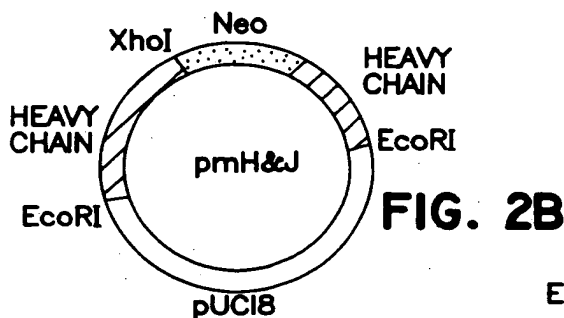


FIG. 2B

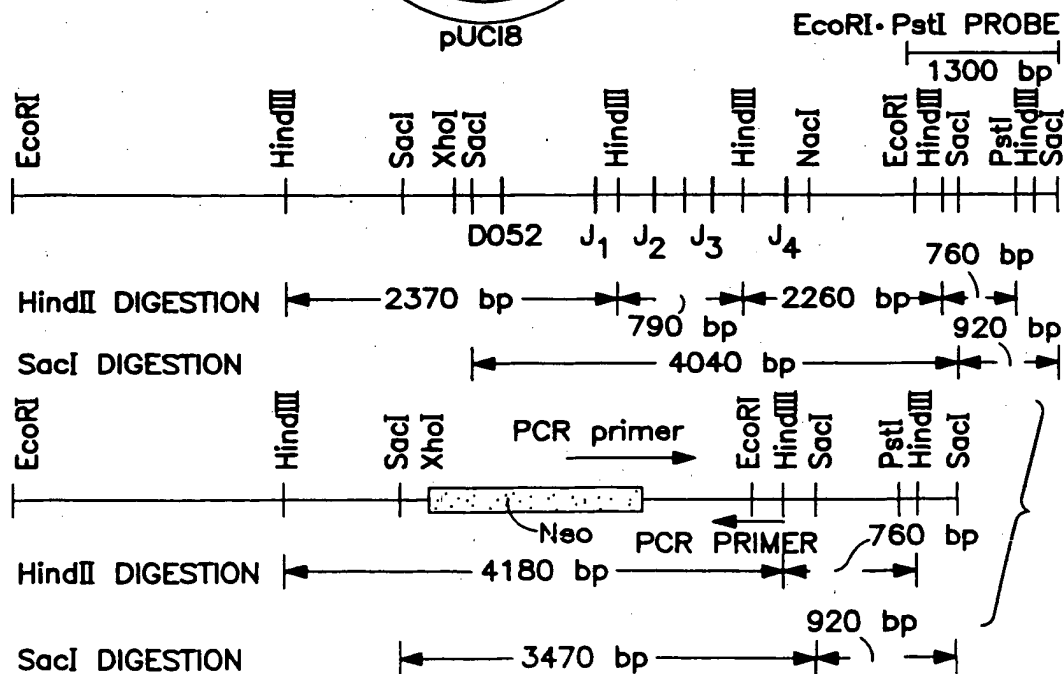
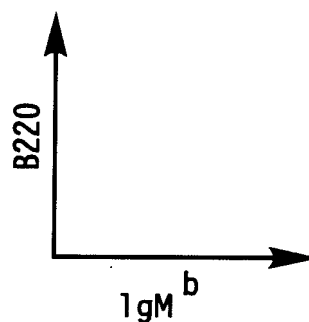
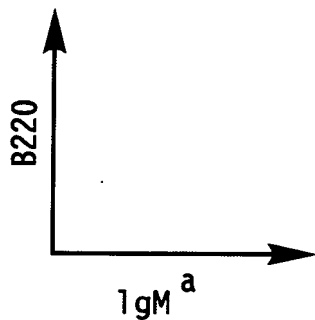
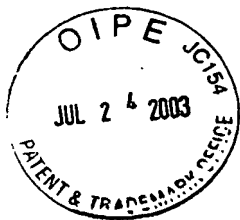
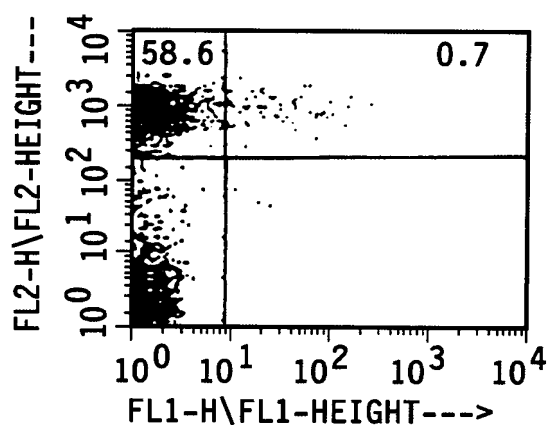
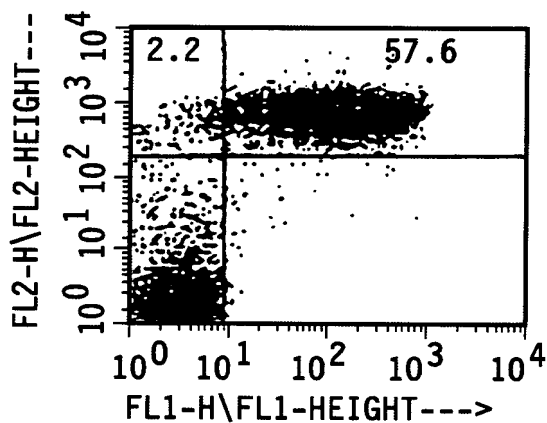


FIG. 2C



a allotype



b allotype

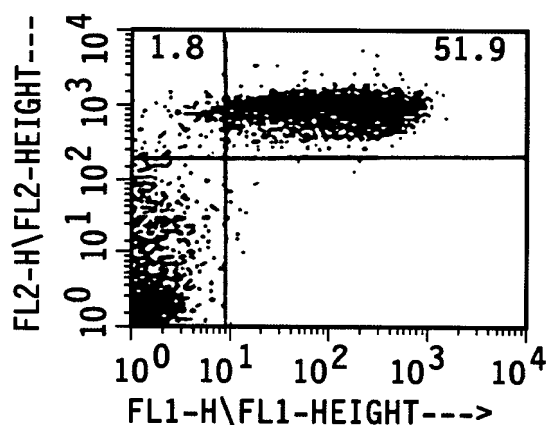
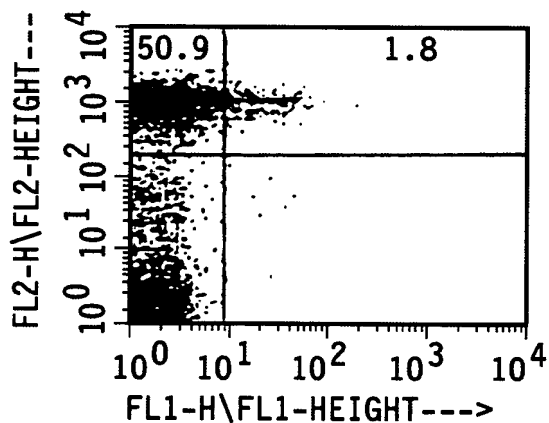
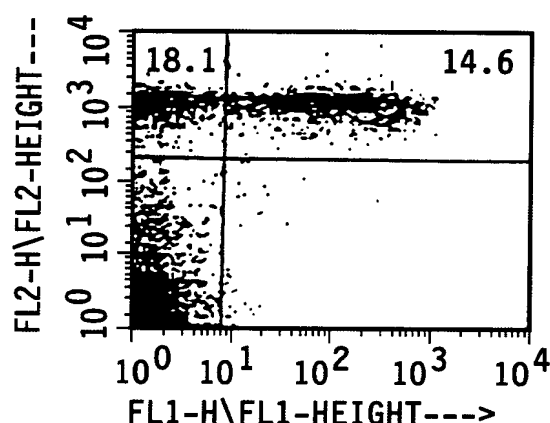
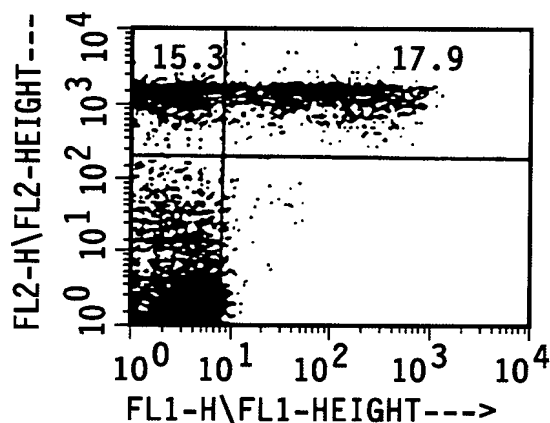


FIG. 3-1



a/bF1



ΔJ_H /bF1

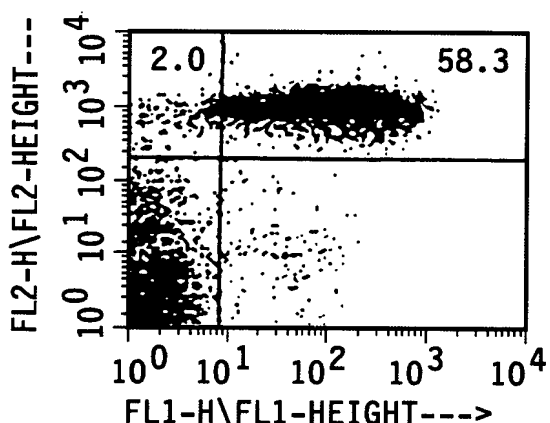
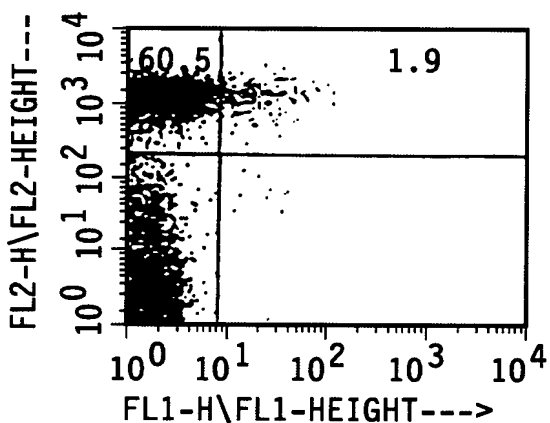


FIG. 3-2

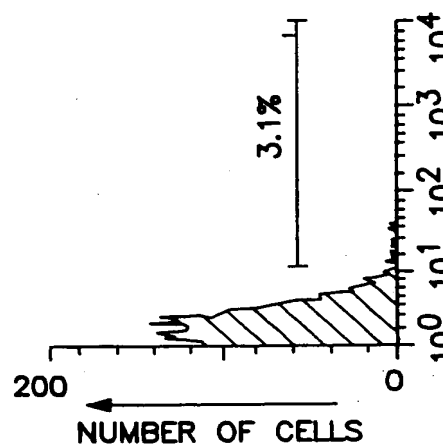


FIG. 4C

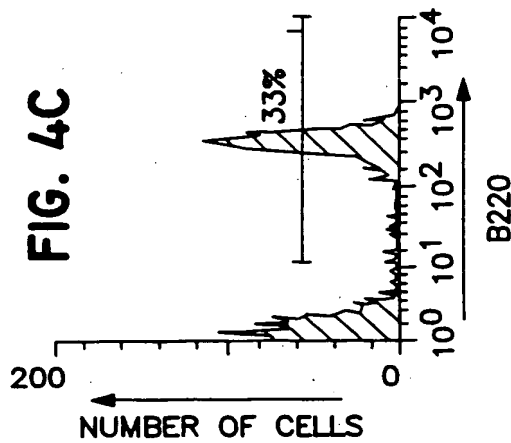


FIG. 4F

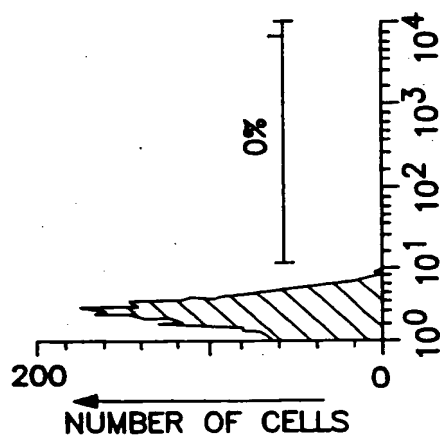


FIG. 4B

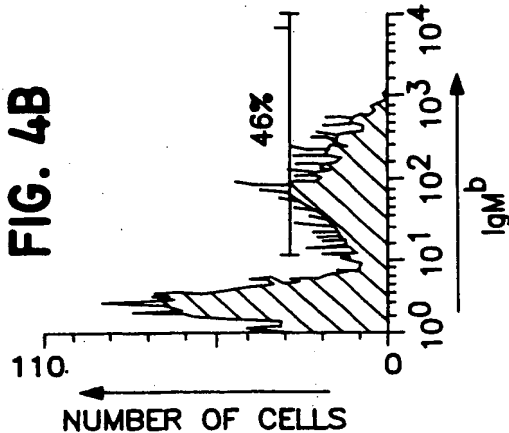


FIG. 4E

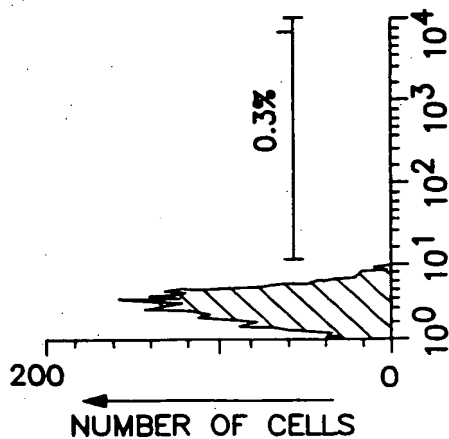


FIG. 4A

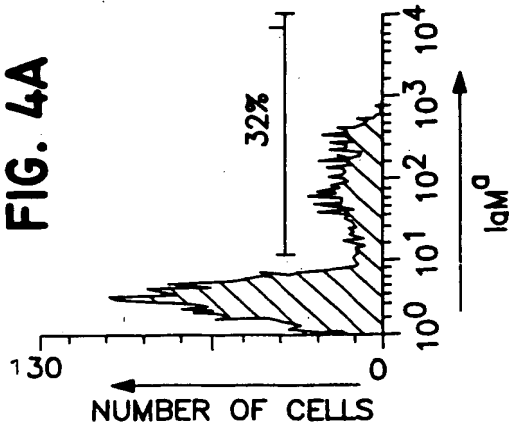


FIG. 4D

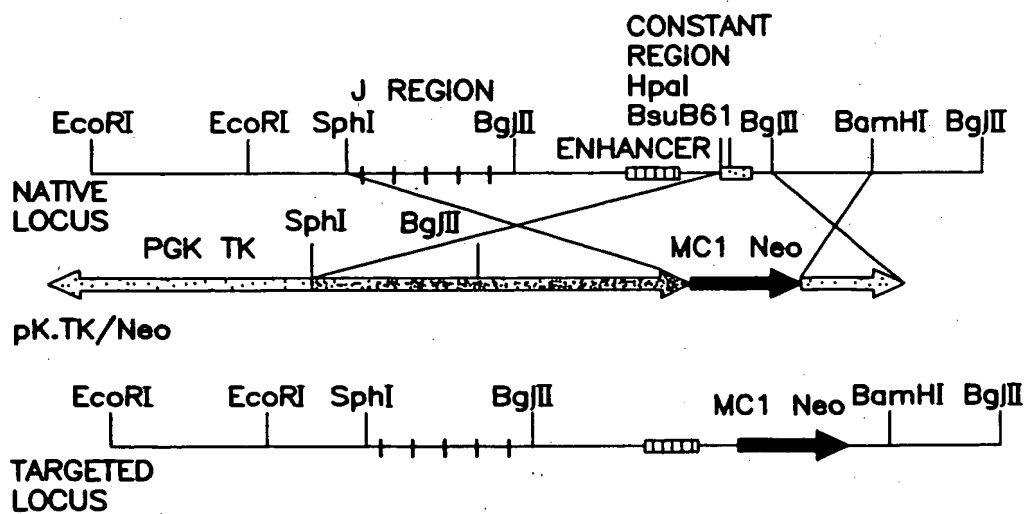


FIG. 5

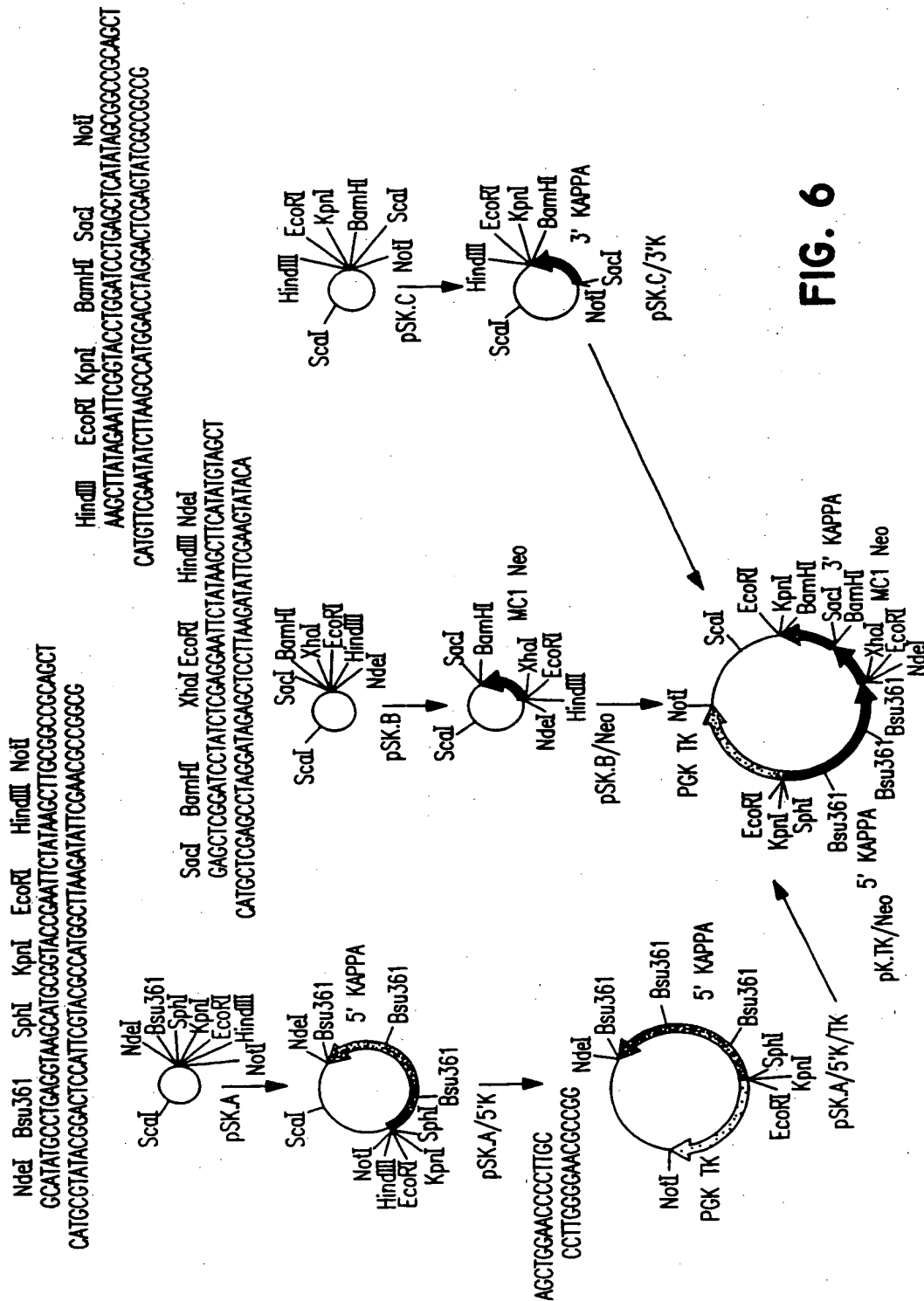


FIG. 6

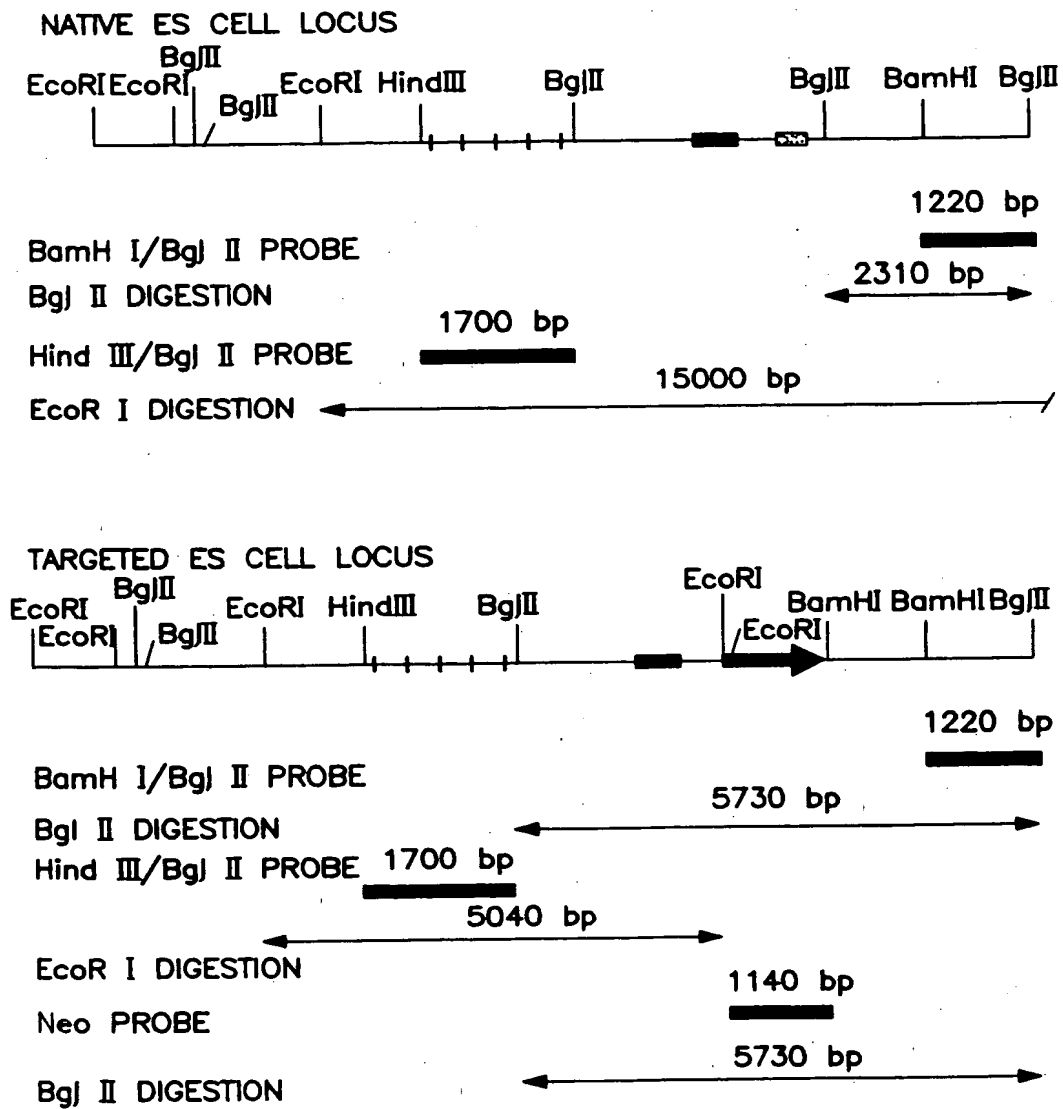
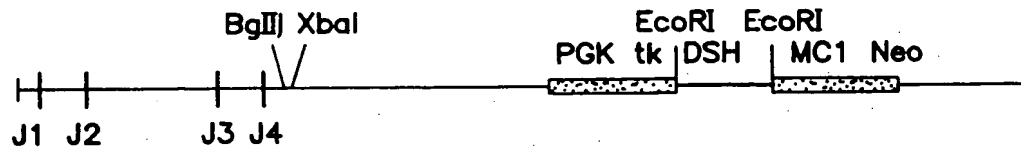


FIG. 7



J REGION KNOCKOUT VECTOR



TARGETING SCHEME

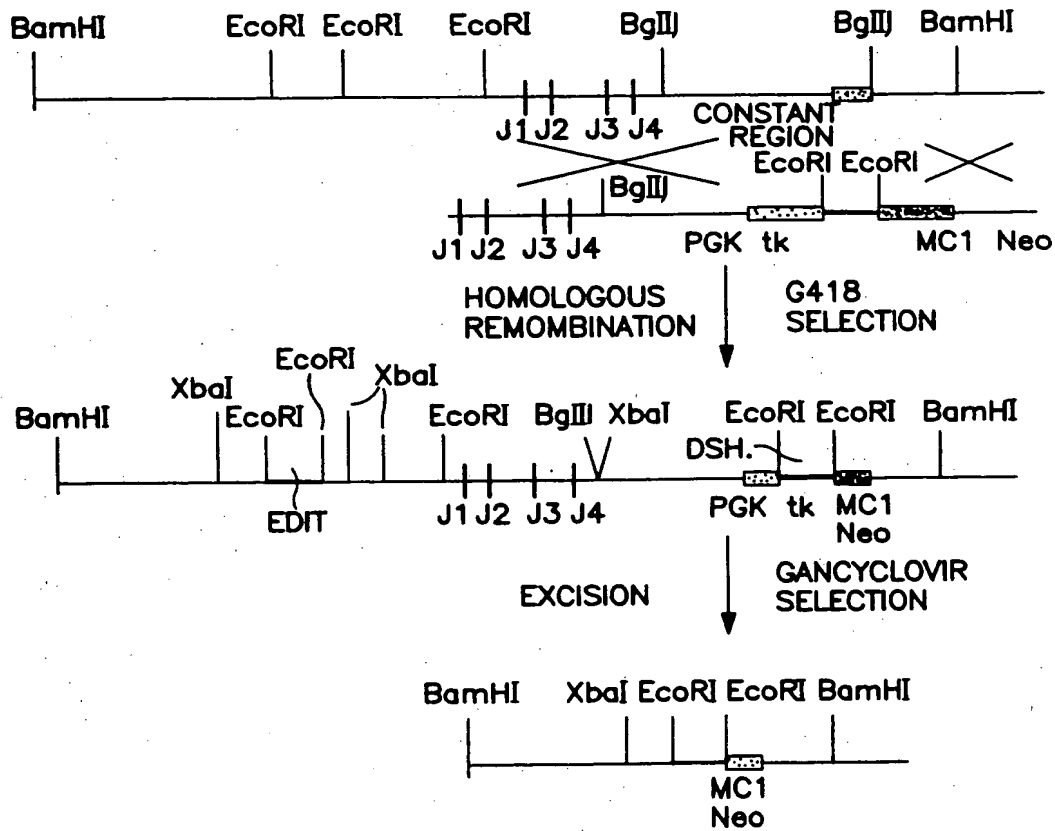


FIG. 8

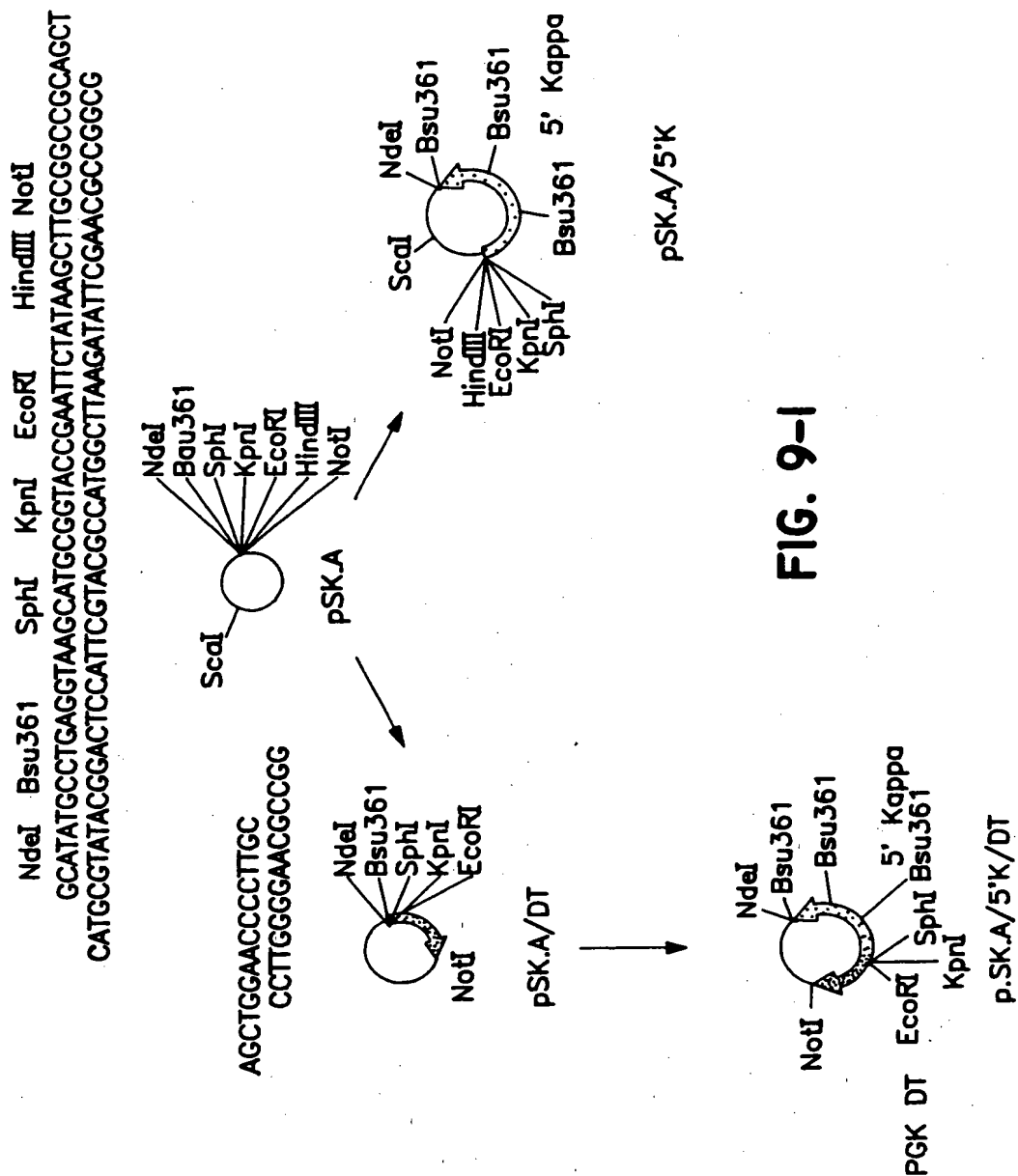


FIG. 9-I



SacI BamHI XhoI EcoRI HindIII NdeI
 GAGCTCGGATCCTATCTCGAGGAATTCTATAAGCTTCATATGTAGCT
 CATCCTCGAGCCTAGGATAGAGCTCCTTAAGATATTCGAAGTATACA

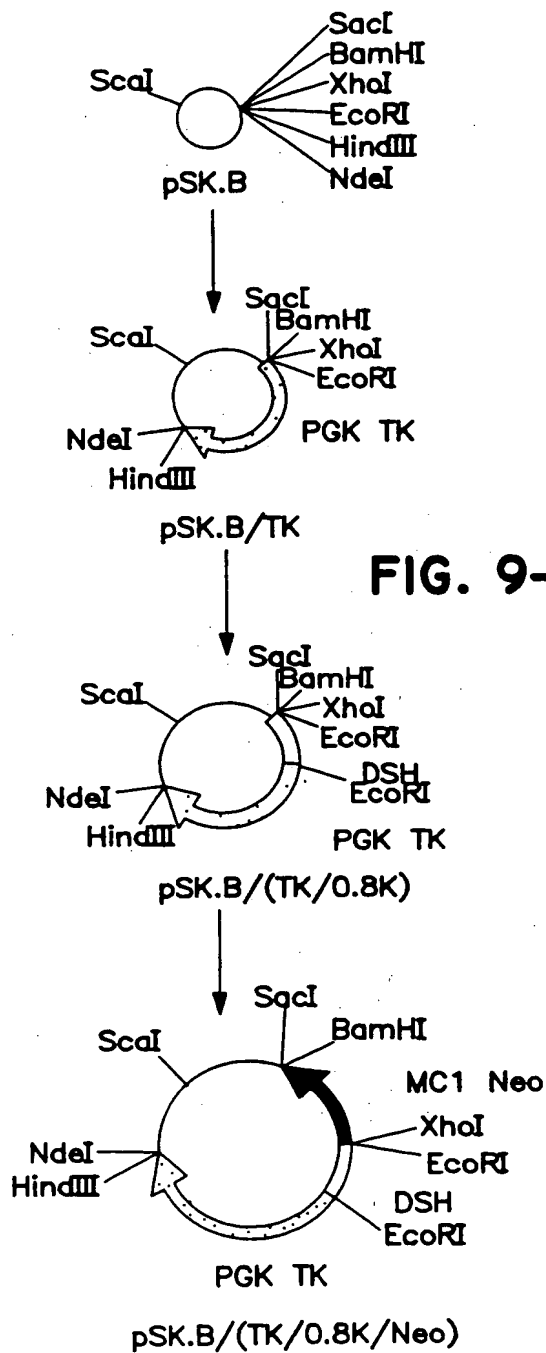


FIG. 9-2



HindIII EcoRI KpnI BamHI SacI NotI
 AAGCTTATAGAATTTCGGTACCTGGATCCTGAGCTCATAGCGGCCGCAGCT
 CATGTTTCAATATCTTAAGCCATGGACCTAGGACTCGAGTATCGCCGGCG

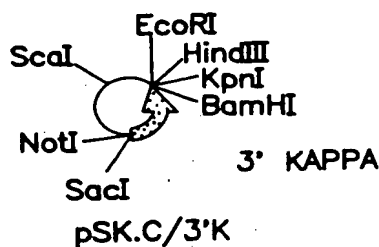
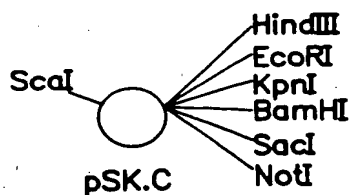
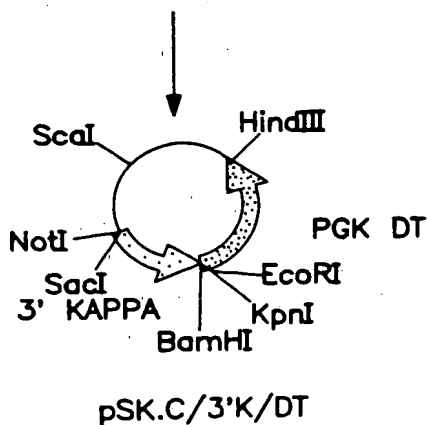
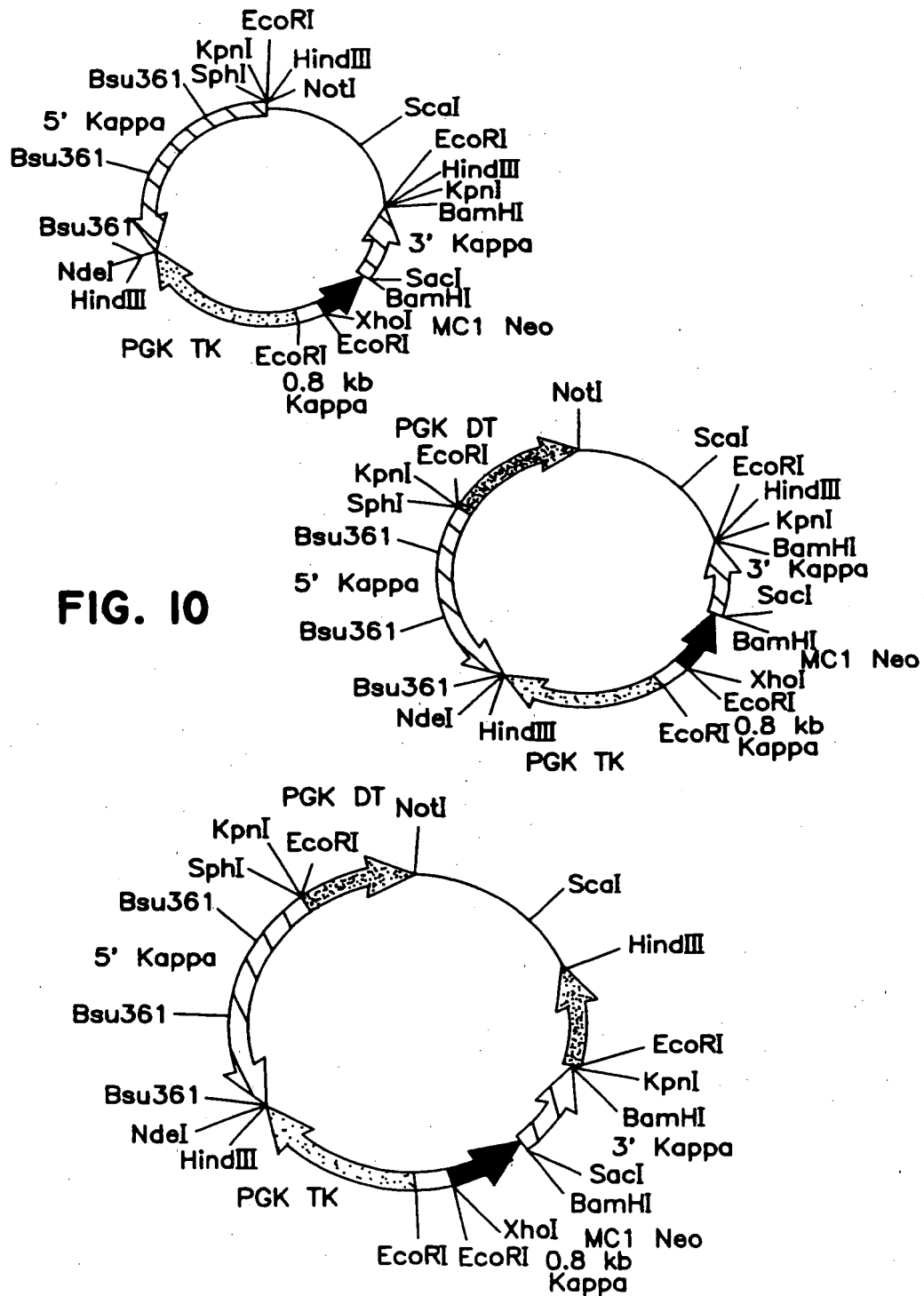
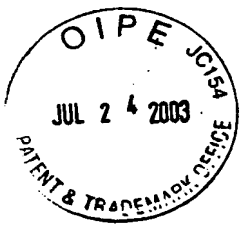


FIG. 9-3





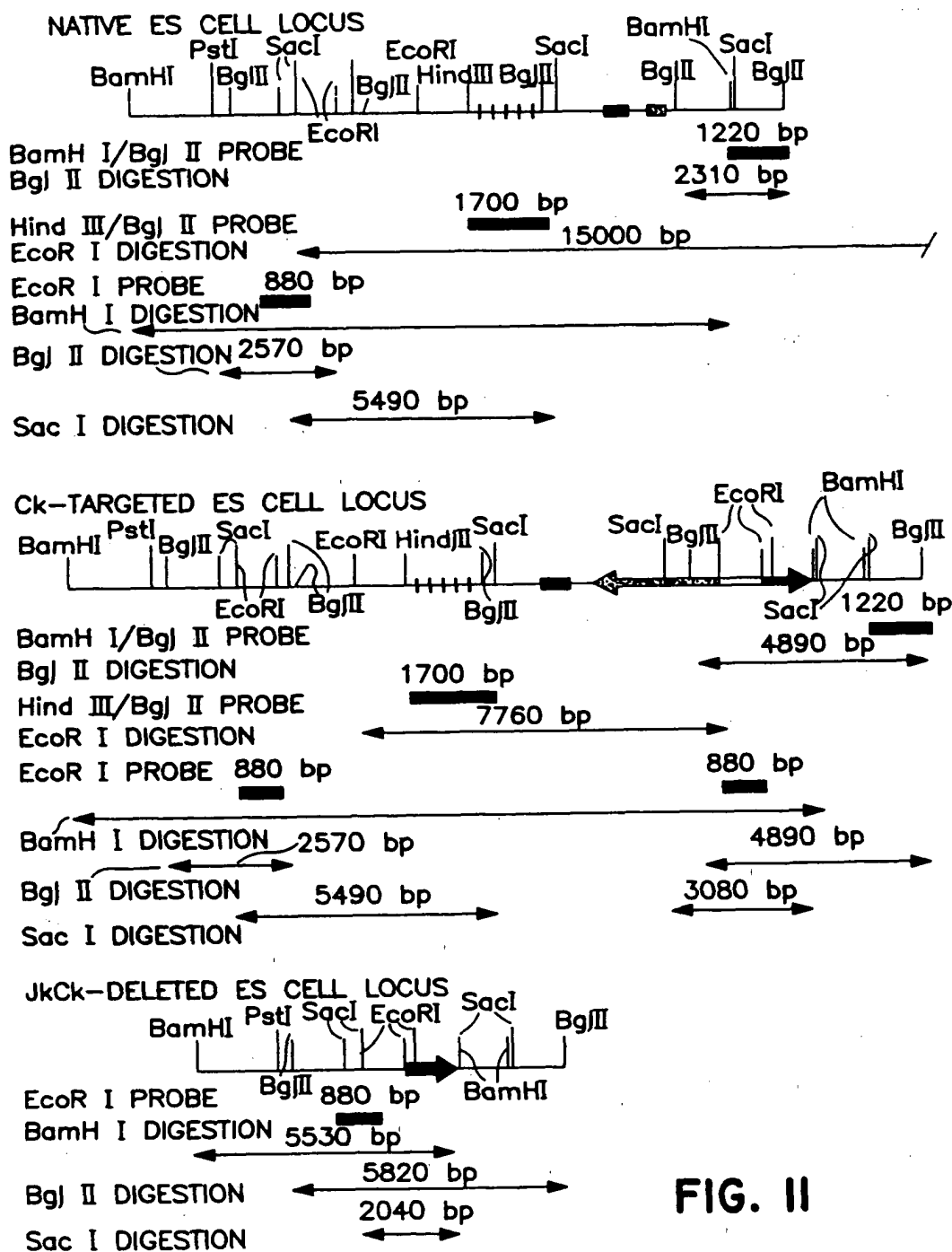


FIG. II



FIG. 12A

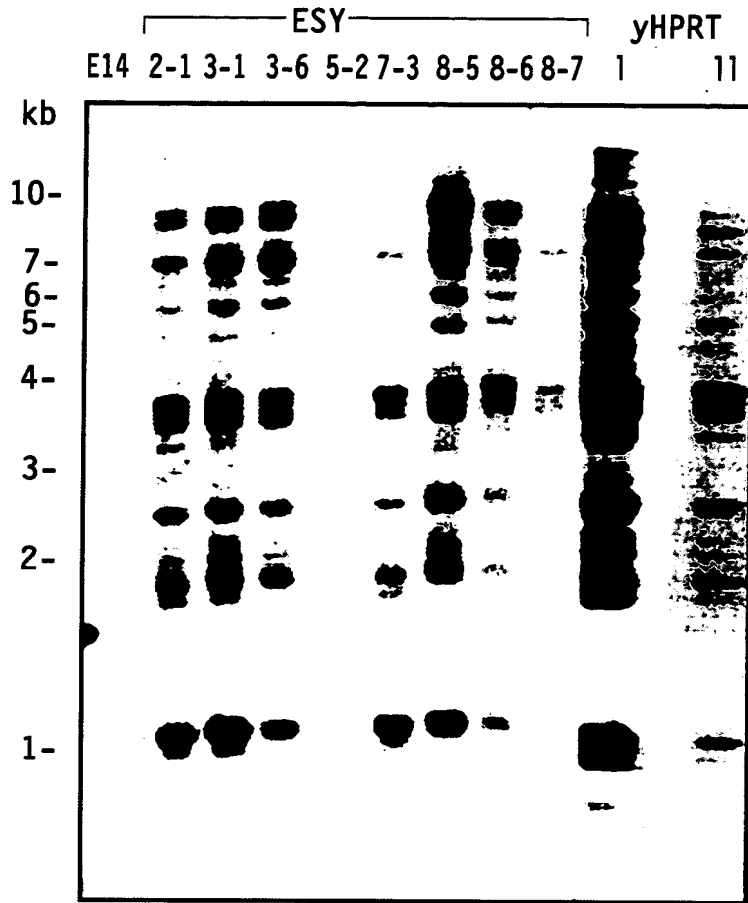
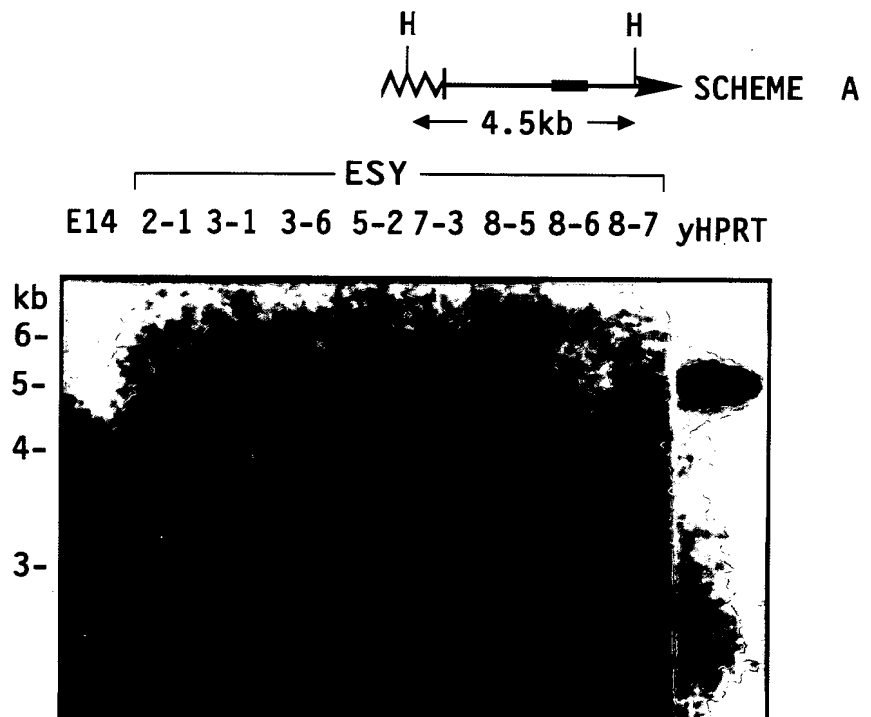


FIG. 12B



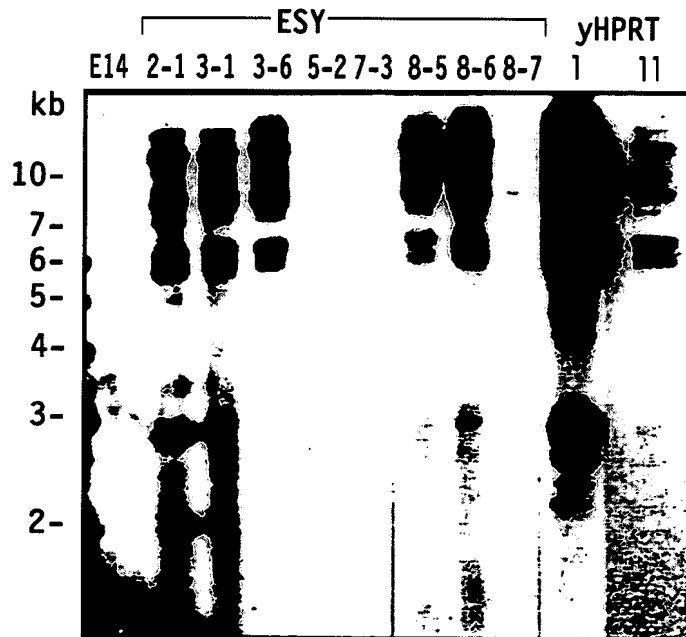
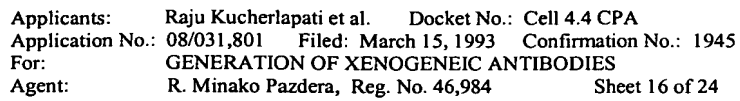


FIG. 12E



FIG. 13A



FIG. 13B

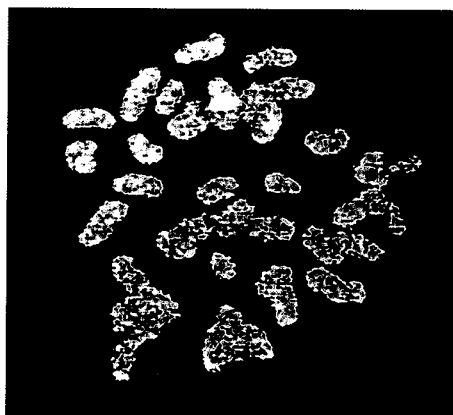
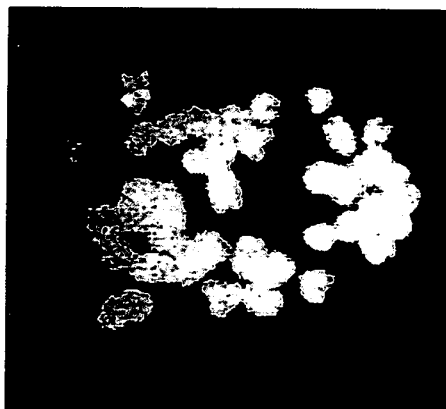


FIG. 13C

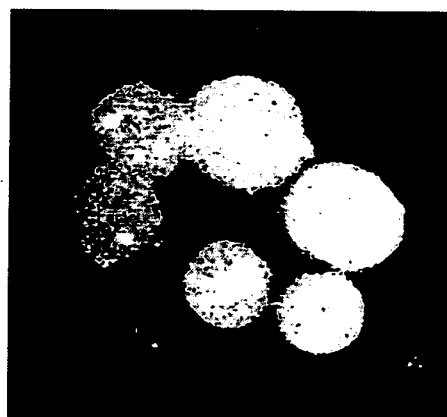


FIG. 13D



FIG. 14A

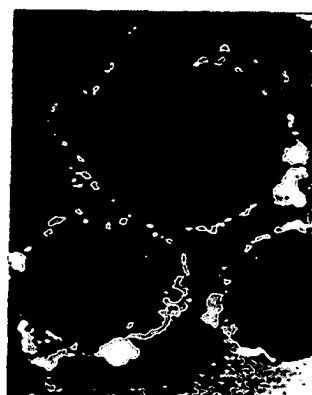


FIG. 14B



FIG. 14C



FIG. 14D

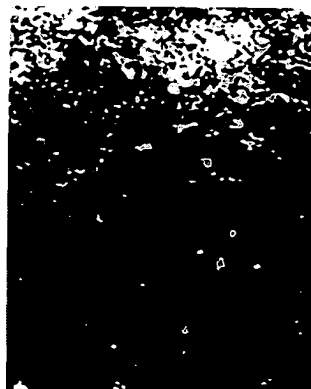


FIG. 14E

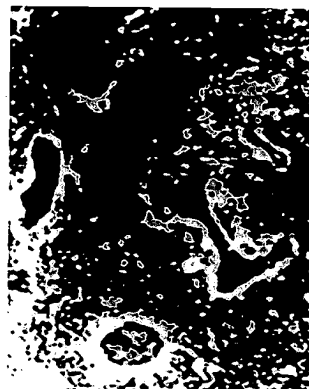


FIG. 14F



Applicants: Raju Kucherlapati et al. Docket No.: Cell 4.4 CPA
 Application No.: 08/031,801 Filed: March 15, 1993 Confirmation No.: 1945
 For: GENERATION OF XENOGENEIC ANTIBODIE
 Agent: R. Minako Pazdera, Reg. No. 46,984 Sheet 19 of 24



FIG. 14I

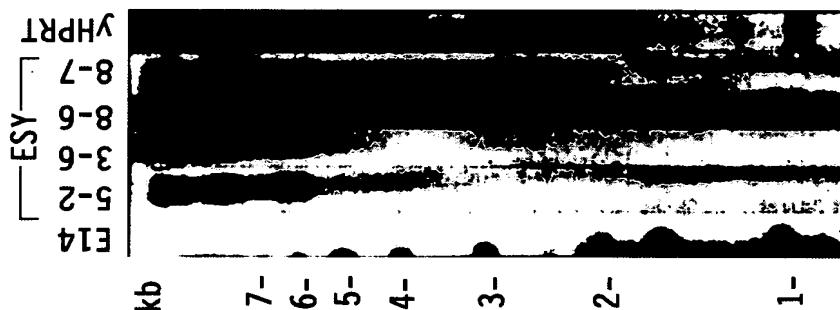


FIG. 14H

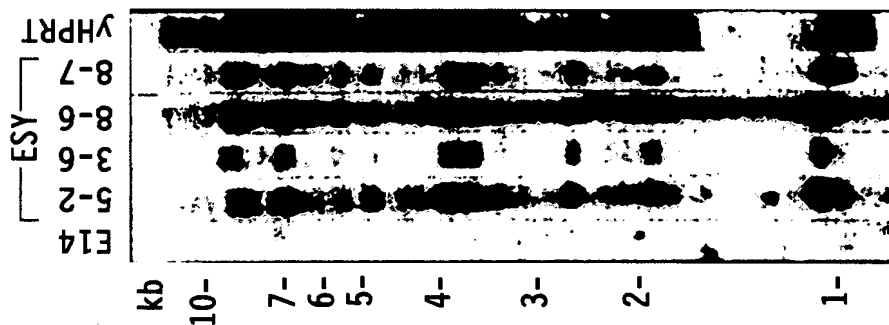
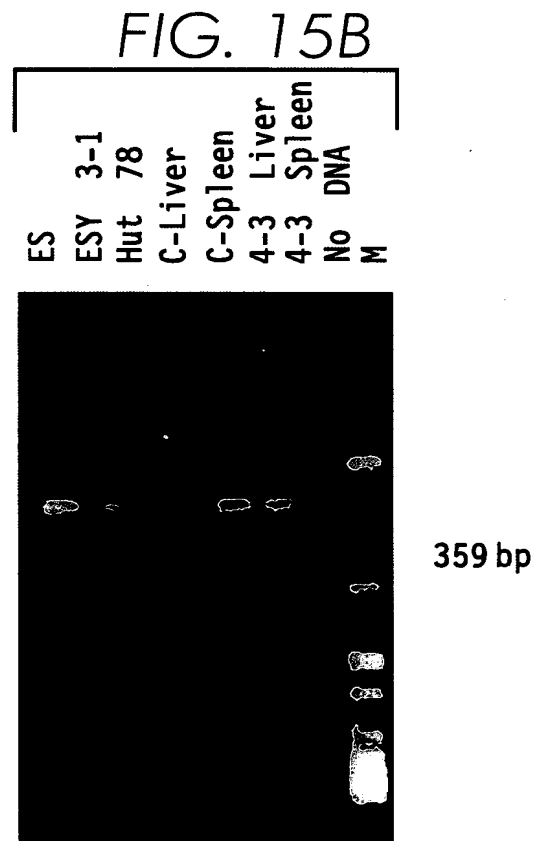
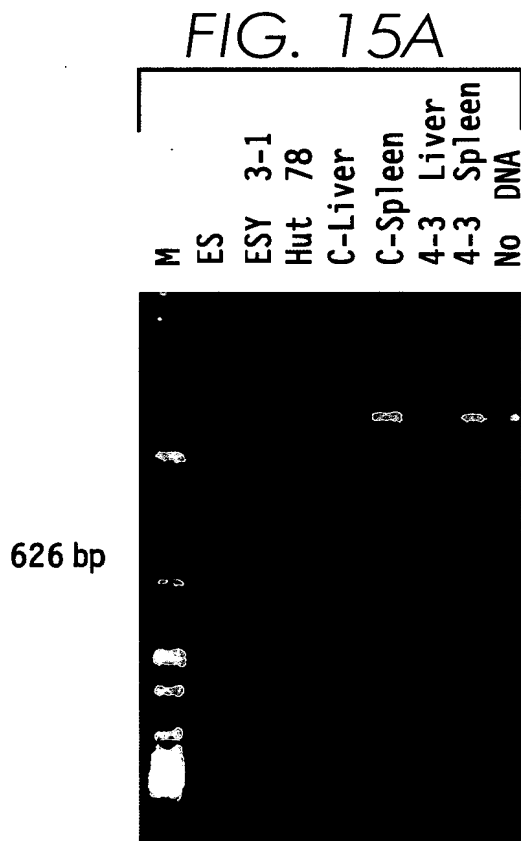
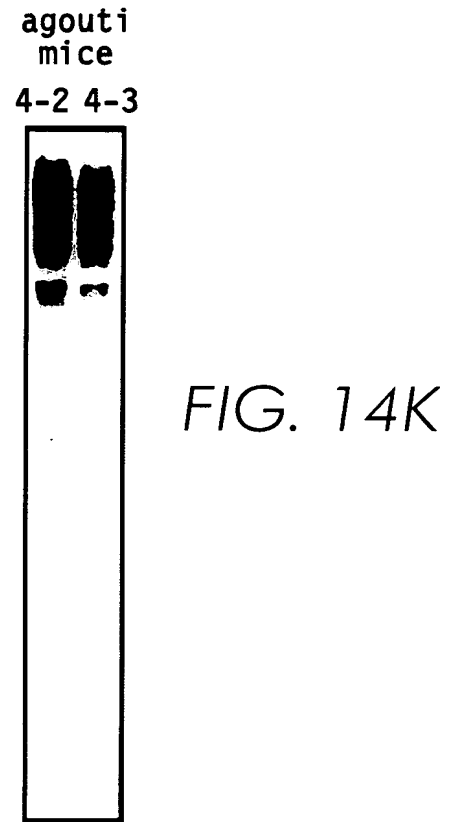
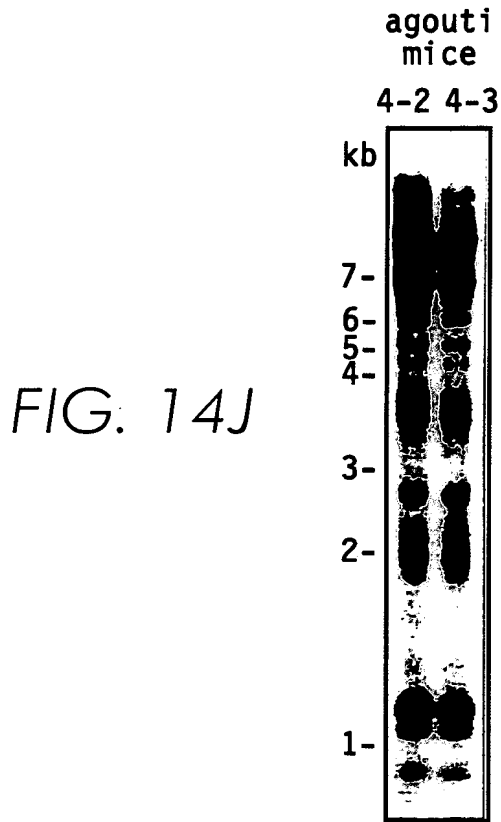
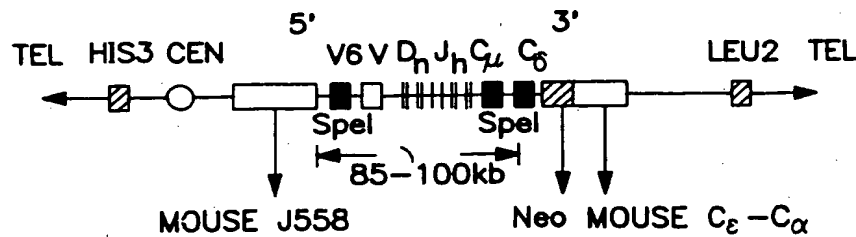
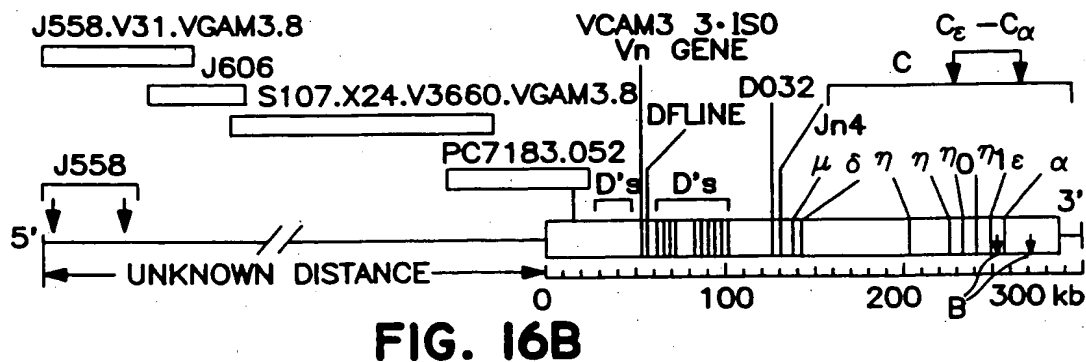
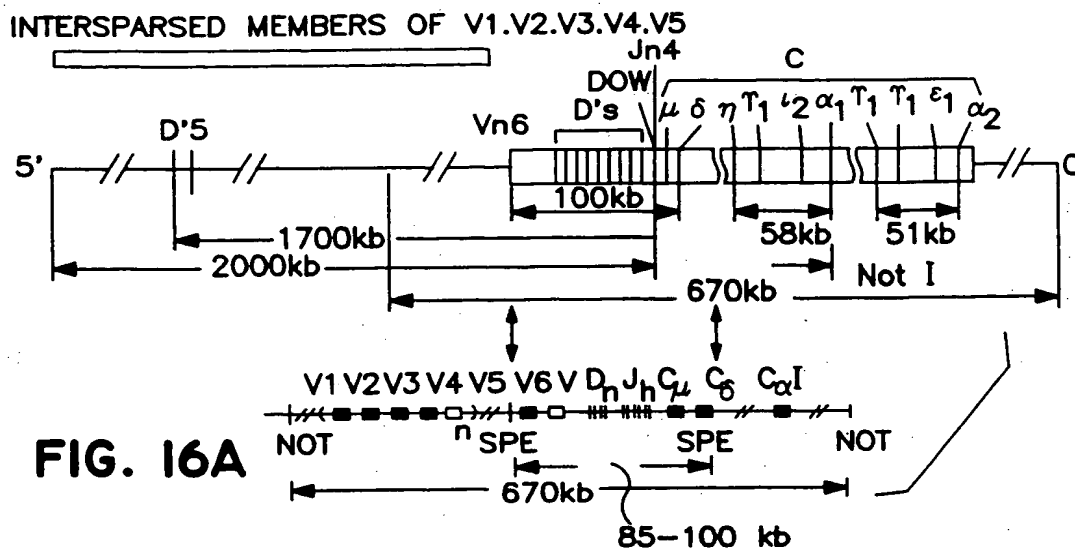
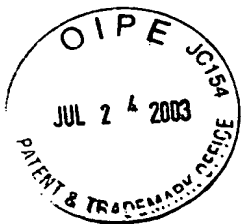


FIG. 14G







Mouse Breeding Scheme

Cross IA.

heterozygous inactive Murine IgH
 X
 heterozygous inactive Murine IgK

<u>MiGh (inactive)</u>	<u>MiGk</u>
<u>MiGH</u>	<u>MiGK</u>
X	
<u>MiGH</u>	<u>MiGk (inactive)</u>
<u>MiGH</u>	<u>MiGK</u>
↓	

F1 (cross I A)

<u>MiGh (inactive)</u>	<u>MiGk (inactive)</u>
<u>MiGH</u>	<u>MiGK</u>

Cross II.

F1 (cross I A) x F1 (cross I B)

F2 Quadruple Heterozygotes

<u>MiGh (inactive)</u>	<u>MiGk (inactive)</u>	<u>HIgH</u>	<u>HIgK</u>
<u>MiGH</u>	<u>MiGK</u>		

Cross III.

Intercross F2 mice

F3 DOUBLE Homozygotes

<u>MiGh (inactive)</u>	<u>MiGk (inactive)</u>	<u>HIgH</u>	<u>HIgK</u>
<u>MiGH (inactive)</u>	<u>MiGK (inactive)</u>		

FIG. 17

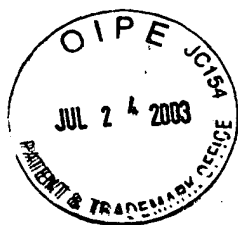
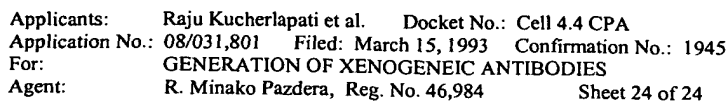


FIG. 18A

MAMMALIAN HOST GENOTYPES

Hetero- or Hemi-zygous Mice	Intercross Product Mice
I. $\frac{\Delta mIgL}{mIgL} \frac{mIgH}{mIgH}$	$\frac{\Delta mIgL}{\Delta mIgL} \frac{mIgH}{mIgH}$
II. $\frac{mIgL}{mIgL} \frac{\Delta mIgH}{mIgH}$	$\frac{mIgL}{mIgL} \frac{\Delta mIgH}{\Delta mIgH}$
III. $\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgH}{hIgH}$	$\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgH}{hIgH}$
IV. $\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgL}{hIgL}$	$\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgL}{hIgL}$
V. Animal I X Animal II	$\frac{\Delta mIgL}{mIgL} \frac{\Delta mIgH}{\Delta mIgH}$
VI. Animal III X Animal V	$\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgH}{hIgH}$ and $\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgL}{hIgL}$
VII. Animal IV X Animal V	$\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgL}{hIgL}$ and $\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgH}{hIgH}$
VIII. Animal VI X Animal VII	$\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgL}{hIgL} \frac{hIgH}{hIgH}$ and $\frac{\Delta mIgL}{\Delta mIgL} \frac{\Delta mIgH}{\Delta mIgH} \frac{hIgL}{hIgL} \frac{hIgH}{hIgH}$



*Not all possible genotypes from intercrosses are shown.

Δ	=	functionally inactive locus
m	=	mouse endogenous gene
h	=	human transgene
IGH	=	immunoglobulin heavy chain
IGL	=	immunoglobulin light chain

FIG. 18B